Amendments to the Specification:

Please replace the paragraph beginning on page 50, line 23, of the specification with the following amended paragraph:

In some embodiments these values can then be used directly as a score, as outlined above and in Equation (1) or Equation (2). The scores can expressed as Pij: the probability of substituting residue i with j. Any transformations of Pij can also be used. Pij can be computed for a specified evolutionary distance. In alternative embodiments, all substitutions with a probability above a certain threshold value may be selected. Threshold values of ~~0.00001,0.00001,0.0001,0.01 or 0.1~~ 0.00001, 0.00001, 0.0001, 0.01 or 0.1 can be used for probabilities and/or threshold values of ~~-5,-4,-3,-2,-1,0,1,2,3,4,5~~ -5, -4, -3, -2, -1, 0, 1, 2, 3, 4 or 5 for any PAM matrix. In still other embodiments, all substitutions with a probability below a certain threshold value may be eliminated. Threshold values of ~~0.00001,0.00001,0.0001,0.01 or 0.1~~ 0.00001, 0.00001, 0.0001, 0.01 or 0.1 can be used for probabilities and/or threshold values of ~~-5,-4,-3,-2,-1,0,1,2,3,4,5~~ -5, -4, -3, -2, -1, 0, 1, 2, 3, 4, or 5 for any PAM matrix. In still other embodiments, the most favorable substitutions can be selected by ranking substitutions in order of their substitution matrix probability scores. For example, the most highly scoring substitution can be selected, or the top 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, up to 50, up to 60, up to 70, up to 80, up to 90, up to 100, up to 110, up to 120, up to 130, up to 140, up to 150, up to 160, up to 170, up to 180, up to 190, up to 200, up to 210, up to 220, up to 230, up to 240, up to 250, up to 260, up to 270, up to 280, up to 290, up to 300, up to 310, up to 320, up to 330, up to 340, up to 350, up to 360, up to 370, up to 380, up to 390, up to 400, up to 500, up to 600, up to 700, up to 800, up to 900, up to 1000, up to 2000, up to 3000, up to 4000, up to 5000, up to 6000, up to 7000, up to 8000, up to 9000, up to 10000, up to 12000, up to 14000, up to 16000, up to 18000 or up to 20000 most highly scoring substitutions can be selected. In still other embodiments, the least favorable substitutions can be eliminated by ranking substitutions in order of their substitution matrix probability scores. For example, the least substitution with the lowest substitution matrix probability may be eliminated, or the 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, up to 50, up to 60, up to 70, up to 80, up to 90, up to 100, up to 110, up to 120, up to 130, up to

140, up to 150, up to 160, up to 170, up to 180, up to 190, up to 200, up to 210, up to 220, up to 230, up to 240, up to 250, up to 260, up to 270, up to 280, up to 290, up to 300, up to 310, up to 320, up to 330, up to 340, up to 350, up to 360, up to 370, up to 380, up to 390, up to 400, up to 500, up to 600, up to 700, up to 800, up to 900, up to 1000, up to 2000, up to 3000, up to 4000, up to 5000, up to 6000, up to 7000, up to 8000, up to 9000, up to 10000, up to 12000, up to 14000, up to 16000, up to 18000 or up to 20000 substitutions with the lowest substitution matrix probability can be eliminated.